33. (Amended) Pharmaceutical composition according to claim 21 for use as a medicament for the treatment of cancer in non-ruminating mammals.

35. (Amended) Method for the treatment of cancer in a human or in a non-ruminating mammal comprising administering to said being in need of such treatment an effective amount of a pharmaceutical composition as defined in claim 21.

REMARKS

The specification has been amended to correct minor clerical errors. No new matter has been entered.

Claim 34 has been canceled, thus rendering moot the 101 rejection. Claims 22-24, 26-29, 32, 33 and 35 have all been amended to depend from claim 21, thus rendering moot the 112 rejection.

Finally, claim 21 has been amended to clarify that the combination provides a synergistic anti-cancer effect.

Turning to the art rejection, all of the claims have been rejected as anticipated by EP '252. As the Examiner is well aware, anticipation under 35 USC 102 can be found only if a reference shows exactly what is claimed. See, for example, *Titanium Metals Corp. v. Banner*, 778 F2d 775, 227 USPQ 773 (Fed. Cir. 1985). It is submitted, EP '252 fails to teach exactly what is claimed. EP '252 teaches the use of inulin and/or oligofructose for the manufacture of a medicament that is suitable for the prevention of mammary carcinogenesis and/or the treatment of breast cancer. EP '252 furthermore discloses on page 3, lines 5 to 6, that said [pharmaceutical] composition may also comprise conventional chemotherapeutic products actively destroying malignant tumor cells. EP '252 stipulates on page 3, lines 6-7, that said conventional chemotherapeutic products are indicated on pages 249 to 253 of the "Repertoire

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Commente des Medicaments", an edition of the "Centre Belge d'Information Pharmacotherapeutique (1989) (document already on file, see IDS mailed January 5, 2002, page 1). On page 3, lines 8 to 20, a list of the classes is indicated in which said chemotherapeutic products are conventionally classified by said "Repertoire Commente", together with a few examples of products for each of said classes.

The disclosure of EP '252 is merely a generic disclosure. Indeed, no specific combination of inulin/oligofructose and a chemotherapeutic product is disclosed, and no indication at all is given in EP '252 regarding a possible selection, method of selection or basis of selection of one or more of said chemotherapeutic products for the manufacture of a pharmaceutical composition.

Admittedly, Example 7 of EP '252 (page 10, lines 41-47) mentions that to determine potential synergistic therapeutic effects, a pharmaceutical composition comprising RAFTILINE® (trade name for chicory inulin of ORAFTI, Tienen (Belgium)) and a conventional chemotherapeutic product actively destroying malignant tumor cells, is prepared and a test is described wherein doxorubicine (an anti-cancer drug of the class of antimitotic antibiotics) was injected into mice fed oligofructose/RAFTILINE® and which were previously inoculated with L1210 leukaemic tumor cells. However, EP '252 is completely silent about the outcome of the test and about possible synergistic anti-cancer effects between inulin and doxorubicine, and, in general, between inulin/oligofructose and conventional anti-cancer drugs.

In EP '252 a synergistic anti-cancer effect between inulin/oligofructose and a chemotherapeutic product is neither disclosed nor suggested and hence the teaching of EP '252 regarding compositions that may contain in addition to the inulin/oligofructose a chemotherapeutic product, has to be seen as compositions seeking the mere addition of the

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effects of both active ingredients. With respect to the combination of the subject claimed invention of inulin/oligofructose and an anti-metabolite anti-cancer drug, EP '252 therefore is a non-enabling disclosure.

Summarizing to this point, EP '252 neither explicitly discloses nor suggests in an enabling manner, a composition according to the present claimed invention containing a combination of inulin and an anti-metabolite anti-cancer drug. Therefore, the subject matter of independent claim 21 cannot be said to be anticipated by EP '252.

It must be remembered the present claimed invention concerns pharmaceutical compositions and their effect on living organisms. Living organisms are notoriously unpredictable, and the effect of pharmaceutical compositions on living organisms also is unpredictable. The claims of the present invention specifically relate to the combination of inulin and an anti-metabolite anti-cancer drug. Amongst the large group of chemotherapeutic products, anti-metabolite anti-cancer drugs form a particular, well delimited class of compounds. The invention, as claimed, is neither disclosed nor suggested within the four corners of EP '252. That is to say, the particular combination of the inulin and an anti-metabolite anti-cancer drug as claimed in the subject application is endowed with special properties that are not taught by the prior art and could not be expected in view of the prior art, namely, that said particular claimed combination would present synergistic anti-cancer properties. As follows from the comparative tests presented in Tables 1 and 2 of the subject patent application, only the claimed particular combinations of inulin/oligofructose and an anti-cancer agent from the class of anti-metabolite anti-cancer drugs present synergistic anti-cancer effects, whereas combinations with inulin/oligofructose with anti-cancer agents from other classes only present additional anti-cancer effects. Accordingly, the claimed combination of inulin/oligofructose and an anti-

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metabolite anti-cancer drug presenting synergistic anti-cancer properties can thus be considered as a selection invention. Indeed the properties of a composition containing a combination according to the present invention are clearly unexpected in view of the prior art, even in view of the generic disclosures on page 3, lines 5-20 and page 10, lines 41-47, of EP '252.

Accordingly, the subject matter of pending claims 21-33 and 35-40 is both novel and non-obvious.

Pursuant to 37 CFR 1.121, marked copies of the specification paragraphs and claims accompany this amendment.

Having dealt with all the objections raised by the Examiner, the application is believed to be in order for allowance. Early and favorable action are respectfully requested.

In the event there are any fee deficiencies or additional fees are payable, please charge them (or credit any overpayment) to our Deposit Account No. 08-1391.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on August 23, 2002 at Tucson, Arizona.

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MARKED SPECIFICATION PARAGRAPHS:

Paragraph beginning at page 2, line 29:

However, most of the anti-cancer drugs have serious disadvantages and drawbacks too. They may present a high degree of toxicity for cells of normal body structures causing, for example, liver and kidney [damages] damage. They may also cause an increased sensitivity to opportunistic infections. Often they also provoke various types of discomfort for the treated person, such as, local necrosis of the body structure in which the drug is parenterally administered, and, when the drug is administered orally or via tube feeding, nausea, vomiting, irritation of the mucoses of the digestive tract and [diarrhoea] diarrhea. In addition to discomfort commonly caused by anti-cancer drugs, anti-metabolic anti-cancer drugs are known to be fairly toxic and to provoke additional discomfort, including megaloblastose, and lesions to the liver or the digestive tract such as stomatitis and buccal and gastro-intestinal ulcers.

Paragraph beginning at page 3, line 3:

The disadvantages and drawbacks may considerably limit the use of available anti-cancer drugs. Indeed, often a curative effective dose of the drug [can not] cannot be given to a patient due to the too high toxicity of the drug to normal cells or to the too high degree of discomfort caused to the patient by the drug.

Paragraph beginning at page 13, line 1:

In all the experiments a chemotherapy potentiating effect has been observed for dietary FOS or inulin. Obviously this therapeutic effect was somewhat different for the various drugs. Only for 5-fluorouracil treatment a synergistic therapeutic effect has [bee] been observed. For treatment with oncovin, endoxan and adriamycin, the therapeutic effects had only additive character. There is no significant difference observed between treatment with inulin or FOS.

MARKED CLAIMS:

21. (Amended) Pharmaceutical composition characterized [in that it comprises] by comprising a combination of an effective dose of inulin and of an anti-metabolic anti-cancer drug, said combination providing a synergistic anti-cancer effect.

22. (Amended) Pharmaceutical composition according to claim [1] 21, wherein the inulin is inulin with a DP up to about 100, or oligofructose or a mixture thereof.

23. (Twice Amended) Pharmaceutical composition according to claim [1] 21, wherein the inulin is chicory inulin with a ($\overline{DP}$) ranging from about 10 to about 30, or oligofructose with a (DP) ranging from 2 to 7 and containing about 5 wt% in total of glucose, fructose and sucrose.

24. (Amended) Pharmaceutical composition according to claim [1] 21, wherein the anti-cancer drug is selected from the group consisting of methotrexate, cytarabin, fluorouracil, mercaptopurin, thioguanin, azathioprin and hydroxycarbamide.

26. (Amended) Pharmaceutical composition according to claim [1] 21, which additionally to the said anti-metabolic anti-cancer drug contains one or more anti-cancer drugs belonging to the class of anti-metabolic anti-cancer drugs and/or to another class of anti-cancer drugs.

27. (Amended) Pharmaceutical composition according to claim [1] 21, in which the inulin and the anti-metabolic anti-cancer drug which constitute the combination are simultaneously present in the same galenic formulation.

28. (Amended) Pharmaceutical composition according to claim [1] 21, in which the inulin and the anti-metabolic anti-cancer drug which constitute the combination are present in separate formulations which together form the pharmaceutical composition.

29. (Amended) Pharmaceutical composition according to claim [1] 21, wherein the single galenic formulation or the separate galenic formulations forming the pharmaceutical composition are suitable for oral, parenteral or rectal administration, or for tube feeding.

32. (Amended) Pharmaceutical composition according to claim [1] 21 for use as a medicament for the treatment of cancer in human.

33. (Amended) Pharmaceutical composition according to claim [1] 21 for use as a medicament for the treatment of cancer in non-ruminating mammals.

35. (Amended) Method for the treatment of cancer in a human or in a non-ruminating mammal comprising administering to said being in need of such treatment an effective amount of a pharmaceutical composition as defined in claim [1] 21.